REMARKS

Claims 1-9, 11-14, 17, 21-22, 32-35 and 37-41 are pending in the instant application. Applicants thank the Examiner for calling to Applicants' attention the inadvertent typographical transposition of the "ARC" number in the elected sequence, SEQ ID NO:107. Applicants, hereby, confirm that SEQ ID NO:107 corresponds to ARC283 (not, ARC 238). Moreover, Applicants note that ARC283 is labeled as SEQ ID NO: 107 at paragraph **[00240]** of the application as filed.

Applicants note the Examiner's admission that SEQ ID NO:107 is free of the art of record.

Applicants respectfully disagree with the Examiner's limitation of claims 13 and 14 to embodiments wherein the first and second aptamers are the same. Applicants submit that no undue search burden is placed on the Examiner by examining claims 13 and 14 as originally filed. A search of the prior art relevant to the patentability of independent claim 1 will yield results that are relevant to embodiments wherein the first and second aptamers, in claims 13 and 14, are non-identical. Applicants respectfully request that the Examiner re-consider this restriction of the claims.

The Examiner rejects all the pending claims. Specifically, the Examiner rejects the claims on the following grounds:

(1) The Examiner rejects claims 14-16 as indefinite under 35 U.S.C. § 112 (second paragraph).

(2) The Examiner rejects claims 1-6, 11-15, 17, 32-35, 37, and 38 under 35 U.S.C. § 112 (first paragraph) as failing to comply with the written description requirement.

(3) The Examiner rejects claims 1-9, 11-14, 17, 21, 22, 32-35 and 37-41 as anticipated, under 35 U.S.C. § 102(b), in view of Pagratis *et al.* (WO 01/09156).

(4) The Examiner rejects claims 1, 32, 37 and 38 as obvious, under 35 U.S.C. § 103(a), in view of Pagratis *et al.* (WO 01/09156).

(5) The Examiner rejects claims 1, 32, 37 and 38 as obvious, under 35 U.S.C. § 103(a), in view of Pagratis *et al.* (WO 01/09156) in view of Cordeiro *et al.* (Invest. Opthamol. Vis. Sci. 40(10): 2225-2234, 1999).

Applicants believe the present amendments, and the following remarks, traverse the Examiner's rejections. These remarks are presented in the same order as they appear above.

1. The Claims Are Definite

The Examiner rejects claims 14-16 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Office Action mailed March 16, 2007, page 3. As a threshold objection, Applicants note that claims 15 and 16 are withdrawn and, therefore, this rejection only applies to pending claim 14. The Examiner rejects this claim for the recitation of the term "type of target" because, "[t]his phrase could refer to different epitopes on the same molecule, or it could refer to different molecules, or to different classes of molecules (i.e. distinguishing enzymes from structural proteins, or proteins from lipids)." Office Action mailed March 16, 2007, page 3.

Applicants respectfully disagree and submit that the claim is definite as presently written. However, in order to further the business interests of Applicants and without acquiescing to the Examiner's argument, while reserving the right to prosecute the original (or similar) claims in the future, Applicants have amended claim 14 such that the target is defined as a protein involved with a disorder of the eye. Applicants note that support for this amendment is found, in one example, at paragraph **[00166]** of the application as filed.[1]

Applicants respectfully request that the pending rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

2. The Claims Are Compliant With The Written Description Requirement Of 35 U.S.C. § 112, First Paragraph

Claims 1-6, 11-15, 17, 32-35, 37 and 38 are rejected under 35 U.S.C. § 112, first paragraph, as not meeting the written description requirement. The Examiner states these claims are rejected as allegedly failing to comply with the written description requirement because the, "[a]pplicants could not have been in possession of the genus of aptamers that bind specifically to any target involved in any way in any disorder of the eye." Office Action mailed March 16, 2007, page 4. Applicants respectfully disagree.

With respect to the written description requirement, "the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991). An

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1 "For example, the target is a protein involved with a pathology, for example, the target protein causes the pathology."

applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997)." MPEP § 2163.02.

Applicants submit that, in view of the standard set out above, the specification as filed provides the statutory requisite of written description in view of the claimed embodiments of the present invention. First, the claimed compositions are literally supported in the specification by an exhaustive description of the selection, minimization, and optimization of aptamers which bind to targets associated with diseases of the eye. See, for example, TGFβ, PDGF and VEGF. Second, Applicants have disclosed (1) features of the genus, (2) functional properties of the genus, and (3) common attributes of the genus. Specifically, the specification describes multiple aptamers directed against targets associated with pathologies of the eye. These pathologies include (but are not limited to):[2] i) trabecular scarring, ii) cell proliferation in glaucoma, iii) age-related maculodegenerative disease, iv) proliferative vitreo-retinopathy and v) proliferative diabetic retinopathy. These sequences are presented throughout the application as filed and are summarized, for example, in Tables 5, 6, and 7 with corresponding functional data presented, in part, at Table 8, 9, and 10. Thus, Applicants have described numerous aptamers that target a variety of proteins associated with disorders of the eye. Moreover, Applicants have identified a common function of these aptamers, namely their ability to not elicit an immune response as compared to other treatment modalities such as monoclonal antibodies.

Applicants submit that the reference to the "over 2000 non-redundant transcripts, novel gene, and splice variants" that Wistow describes in the human eye is not relevant to the instant written description analysis. Office Action mailed March 16, 2007, page 4. That is to say, Applicants are under no obligation to parse out, as the Examiner suggests, which one of Wistow's transcripts are involved in eye disease or which gene products of the eye are involved in eye disease in order to satisfy the written description requirement in view of the claimed embodiments of the present invention. The subject matter of the claim need not be described literally (i.e., using the same terms or in *haec verba*) in order for the disclosure to satisfy the description requirement." MPEP § 2163.02. Thus, Applicants submit the claims are sufficiently described by the application

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2 The elements in this list are found in the Application as originally filed at paragraphs **[00120], [00170], [00127], [00127] and [00127].**

as filed in such a manner as to allow a person skilled in the art to conclude that Applicants had possession of the claimed invention at the time of filing. Applicants respectfully request, therefore, that the written description rejection be withdrawn.

3. The Claims Are Not Anticipated

The Examiner has rejected claims 1-9, 11, 13, 14, 21, 22, 32-35, 37, 40, and 41 under 35 U.S.C. § 102(b) as anticipated by WO 2001/09156 to Pagratis *et al.* Applicants respectfully disagree. The MPEP states that "to anticipate a claim, the reference must teach every element of the claim." Emphasis added, MPEP § 2131. Additionally, "[t]he rule is that the burden of persuasion is on the PTO to show why the applicant is not entitled to a patent." In re Epstein, 31 USPQ2d 1817, 1825 (Fed. Cir. 1994) (Plager, J. joined by Cowen, J., concurring.) (citing to *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992) (Plager, J., concurring); *In re Warner*, 379 F.2d 1011, 1016, 154 USPQ 173, 177 (CCPA 1967), *cert. denied*, 389 U.S. 1057(1968)). "[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant . . . . If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Specifically, the Examiner states, "[t]he functional limitations recited in the claims are considered to be inherent in the structures of the aptamers of Pagratis. Since Pagratis taught aptamers that bind specifically to TGFbeta-2, the effects of binding are inherent absent evidence to the contrary." Office Action mailed March 16, 2007, page 6. Pagratis *et al.*, however, are completely silent on the use of any aptamer described in WO 2001/09156 as a composition for treatment of a disorder of the eye comprising an aptamer which binds specifically to a target involved in said disorder. An art reference may be held not to anticipate the claimed subject matter if it is found not to be sufficiently enabling, in other words, if it does not place the subject matter of the claims within the possession of the public. See, *In re Wilder*, 166 USPQ 545, 548 (C.C.P.A. 1970). Given that the functional characteristics (*i.e.*, the use of an aptamer in the treatment of an eye disorder) of Applicants' pending claims were elucidated by means of extensive experimentation, Applicants submit the same as "evidence to the contrary" to prove that the

compositions described by Pagratis *et al.* do not inherently teach the functional limitations of the pending claims.

In view of the above, therefore, Applicants respectfully submit the pending rejection, under 35 U.S.C. § 102(b), be withdrawn.

4. and 5. The Claims Are Not Obvious

The Examiner has issued two rejections under 35 U.S.C. § 103(a) (each of the rejections is discussed in further detail below). Applicants respectfully and submit the combination of references, referred to by the Examiner, fails to provide *a prima facie* showing of obviousness as required by § 2143 of the MPEP. There are three criteria that must be met to provide *prima facie* obviousness. The first of these criteria is a suggestion or motivation in the references or the knowledge generally available to combine the reference teachings. The second criterion is the prior art must teach or suggest all the claim limitations. The third criteria is a reasonable expectation of success should the combination be carried out. Applicants submit that the Examiner has failed to set forth *a prima facie* case of obviousness because these criteria have not been met.

A. Claims 1, 32, 37 and 38 Are Not Obvious

The Examiner has rejected Claims 1, 32, 37 and 38 under 35 U.S.C. § 103(a) as allegedly obvious in view of Pagratis *et al.* Office Action mailed March 16, 2007, page 6. In particular, the Examiner states a linear arrangement of PEG-first aptamer-PEG-second aptamer, ". . .would have been obvious to one of ordinary skill in the art because Pagratis taught single PEGylated aptamers, as well as aptamers joined by a PEG linker, so the decision to link to pegylated aptamers together to obtain a linear arrangement of PEG-first aptamer-PEG-second aptamer is simply a matter of design choice." Office Action mailed March 16, 2007, page 7. Applicants respectfully disagree.

The Examiner is reminded that the fact that the prior art may be modified, in the manner suggested by the Examiner, does not make the modification obvious unless the prior art suggested the desirability of the modification. See, *In re Fritch*, 23 USPQ 2d 1780, 1783–84 (Fed. Cir. 1992). By the Examiner's own admission, however, "Pagratis did not teach a composition comprising a linear arrangement of PEG-first aptamer-PEG-second aptamer." Office Action mailed March 16, 2007, page 7. Given the Examiner only cites to Pagratis *et al.* to support this first rejection under 35 U.S.C. § 103, Applicants submit there is insufficient evidence to

maintain this obviousness rejection. Moreover, Applicants note that the Examiner's assumptions do not constitute the disclosure of the prior art. *See*, In re Rijckaert, 9 F.3d 1531, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). Accordingly, the pending obviousness rejections should be withdrawn.

B. Claims 1, 11 and 12 Are Not Obvious

The Examiner rejects claims 1, 11 and 12 under 35 U.S.C. § 103(a) as allegedly unpatentable over Pagratis *et al.* in view of Cordeiro *et al.* Office Action mailed March 16, 2007, page 7. In particular, the Examiner states, "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to use both the aptamer of Pagratis and either or both of the antibody or mitomycin C of Pagratis together in the same composition to treat glaucoma. " Office Action mailed March 16, 2007, page 8.

Applicants respectfully disagree and submit that the Examiner has failed to establish a *prima facie* case of obviousness because the cited references do not provide a motivation to combine the references with a reasonable expectation of success. Furthermore, Applicants submit the Examiner offers documentary statements about the art in place of the requisite showing of how the cited art could motivate the skilled artisan to arrive at the claimed embodiments of the present invention. The Examiner states that, "Cordeiro taught that a monoclonal antibody against TGFbeta-2 was useful. . .[and]. . .Pagratis found that an anti-TGFbeta-2 aptamer inhibits the TGFbeta-2 bioactivity with a potency equivalent to that of a monoclonal anti-TGFbeta-2 antibodies." Office Action mailed March 16, 2007, page 8.

Applicants respectfully submit these observations, about the cited art, cannot support the Examiner's conclusion that, "[i]n view of the teachings of Cordeiro and Pagratis, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in using the aptamers of Pagratis to treat glaucoma." Office Action mailed March 16, 2007, page 8. Accordingly, the pending obviousness rejections should be withdrawn.

CONCLUSION

Applicants submit the amendments and arguments set forth above traverse the Examiner's rejections and, therefore, request that these rejections be withdrawn and the pending claims be passed to allowance. Should the Examiner believe a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at: 617.542.6000.

Respectfully submitted,

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